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uni-
(b) at least a second vector that is capable of expressing flavivirus structural protein(s) and/or any other proteins required for packaging of the replicon into infectious flavivirus-like particles.

6. A gene expression and delivery system comprising:

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con-
(a) a self-replicating expression vector of flavivirus origin which includes the nucleotide sequence for the flavivirus 5'UTR, at least a portion of the 5' nucleotide coding region for flavivirus core protein, the nucleotide coding region for flavivirus non-structural proteins, a sufficient amount of the 3'-terminal region of the flavivirus 3'UTR required for self-replication of flavivirus genomic material wherein (i) the vector is adapted to receive at least a nucleotide sequence without disrupting the replication capabilities of the vector, (ii) the nucleotide sequence is inserted into the vector in a manner which deactivates expression of at least a gene that would otherwise code for a flavivirus structural protein and (iii) the inserted nucleotide sequence does not encode the structural protein sequence that it deactivates; and

(b) at least a second vector that is capable of expressing the flavivirus structural protein(s) that is not expressed by the self-replicating expression vector described in (a).

A3
11. A gene expression and delivery system according to claim 6 wherein the nucleotide sequence is inserted in place of at least a deleted gene encoding a structural protein.

22. A gene expression system according to claim 21 wherein the replicon is derived from the FLSD or FLSDX clones.

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23. A gene expression system according to claim 21 wherein the replicon is selected from one of the following vectors: C20rep; C20DXrep; C20DXrepNeo; C20DX2Arep; C20DX2ArepNeo; C20DX/CAT/2Arep; C20DX/CAT/2ArepNeo; C20DXIRESrep; C20DX/CAT/IRESrep; C20DX/GFP/2Arep; C20DX/GFP/2ArepNeo;

all cases
C20DX/hcvCORE160/2Arep; C20DX/hcvCORE191/2Arep; C20DX/hcvNS3/2Arep;
25 Bk
C20DX/VSV-G/2Arep; C20DX/~~B-GAL~~/2Arep; C20DXUb2A_HDVrep or pKUNRep1.

37. A gene expression system according to claim 1 wherein the replicon encodes all flavivirus structural proteins except for flavivirus core protein and the second vector is SFV-C.

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40. A flavivirus replicon selected from the following: C20DX2Arep;
C20DX2ArepNeo; C20DX/CAT/2Arep; C20DX/CAT/2ArepNeo; C20DXIRESrep;
C20DX/CAT/IRESrep; C20DX/GFP/2Arep; C20DX/GFP/2ArepNeo;
C20DX/hcvCORE160/2Arep; C20DX/hcvCORE191/2Arep; C20DX/hcvNS3/2Arep;
C20DX/VSV-G/2Arep; C20DX/B-GAL/2Arep; C20DXUb2A_HDVrep or pKUNRep1.

an
43. A method for producing a stable cell line capable of persistently producing replicon RNA'S, comprising the steps of:

(i) introducing into a cell a replicon of flavivirus origin which is adapted to receive at least a nucleotide sequence without disrupting its replication capabilities and which is unable to express at least part or all of a structural protein(s) region; and

(ii) culturing that cell line under conditions which permit cell growth and replication.

44. A method for producing a flavivirus like particles comprising the steps of:

(i) introducing into a cell a replicon of flavivirus origin which is adapted to receive at least a nucleotide sequence without disrupting its replication capabilities and which is unable to express at least part or all of a structural protein(s) region;

(ii) introducing into a replicon-containing cell a second vector that is capable of expressing flavivirus structural protein(s) and/or any other proteins required for packaging of the self-replicating expression vector into flavivirus viral particles which vector is engineered to prevent recombination with the self-replicating vector when in its presence; and

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(iii) harvesting virus like particles containing the replicon.

46. A flavivirus like particle according to claim 45 wherein said particle contains a replicon that is derived from a DNA based replicon vector.

48. A DNA based replicon vector of flavivirus origin, wherein the vector comprises:

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(a) a complementary DNA sequence of flavivirus origin that is adapted to receive at least a nucleotide sequence without disrupting its replication capabilities and which is unable to express at least part or all of a structural protein(s) region and or a protein(s) or part thereof required for packaging of a flavivirus genome into a virus-like particle; (b) a mammalian expression promoter 5' to the complementary DNA sequence of flavivirus origin; and (c) at least a second nucleotide sequence capable of terminating transcription of replicon RNA with a precise 3' terminus; and wherein the promoter and the second nucleotide sequence are capable of promoting transcription and terminating same, of flavivirus RNA within the nucleus of a transfected cell.

49. A DNA based replicon vector according to claim 48 wherein the complementary DNA sequence of the nucleotide sequence includes a flavivirus 5' untranslated region (UTR), at least a portion of the 5' coding region for flavivirus core protein, the nucleotide sequence coding for the flavivirus non-structural proteins, and part or all of the 3'-terminal sequence of a flavivirus 3'UTR, required for self-replication of flavivirus genomic material, which vector is adapted to receive at least a nucleotide sequence without disrupting its replication capabilities.

50. A DNA based replicon vector according to claim 48 wherein the nucleotide sequence is inserted in place of at least a deleted structural gene.

Remarks

Claims 1, 6, 11, 22, 23, 37, 40, 43, 44, 46, 48, 49 and 60 have been editorially amended in order to address the Examiner's various concerns. Upon entry of this amendment, claims 1-65 will remain pending and in condition for allowance.